DEPARTMENT OF HEALTH & HUMAN SERVICES M970N Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 3 1997

WARNING LETTER

VIA FEDERAL EXPRESS

Mr. Keiichiro Tomita
President
Radia Industry Co. Ltd.
168 Ooyagi
Takasaki, Gunma, 370 Japan

Dear Mr. Tomita:

During the Food and Drug Administration's (FDA) inspection of your firm, Radia Industry Co. Ltd., located at 168 Ooyagi, Takasaki, Gunma 370, Japan from February 24-27, 1997, our investigator determined that your firm sterilizes plasma separators. Plasma separators are devices within the meaning of Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated, in that the methods used in, or the facilities or controls used for the manufacture, packaging, storage, or installation are not in conformance with the Medical Device Good Manufacturing Practice regulations, as specified in Title 21, Code of Federal Regulations (21 CFR), Part 820, as follows:

1. Failure to conduct processing control operations in a manner designed to assure that the device conforms to applicable specifications, as required by 21 CFR 820.100(b)(2). For example, there was also an incorrect maximum conveyor speed observed on February 24, 1997, by the investigator and one member of the firm. An operator is required to manually change the upper and lower limits of the speed to insure that the correct absorbed dose is delivered. The computer software is supposedly designed to prompt the operator when a change in conveyor speed is necessary.

2. Failure of the quality assurance program to identify, recommend, or provide solutions for quality assurance problems and verify the implementation of such solutions. For example:

   a. The firm failed to investigate why their polymethylmethacrylate (PMMA) dosimeters occasionally are found to have significant variability in absorbance depending on which side (front or back) they are read in the spectrophotometer. The firm had no explanation for this disparity.

   b. No investigation has been done to determine why Radix Batch 5 dosimeters may have significantly differing absorbance values depending on which side the absorbance is read. Reportedly, this occurs in about 1% of the dosimeters. Absorbance differences have been seen up to 80 units (e.g. dosimeter E-503).

3. Failure of the quality assurance program to assure that all quality assurance checks are appropriate and adequate for their purpose and are performed correctly, as required by 21 CFR 820.20(a)(4). For example, the calibration curve for Batch #5 of Gammachrome YR dosimeters was generated in February 1995. The same curve was used to obtain absorbed dose values for dosimeters from this batch for the February 1997, quarterly FS-Plasma Separator dose verification study.

4. Failure to control environmental conditions such as temperature to provide proper conditions for storage of the plasma separators as required by 21 CFR 820.46. For example, the plasma separators are labeled for storage at between 5-30° C. Pre and post irradiation storage temperatures are not controlled in that temperatures may fall below 5°C in an area central to the separator storage location. Temperatures are generally dependent on outside ambient temperatures.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the close of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions. Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts.

We acknowledge that you have submitted a response dated March 17, 1997, concerning our investigator's observations noted on the form FDA 483. We have reviewed your response and are unable to determine the adequacy of your response. In order to evaluate your response to the FDA-483, it will be necessary for you to submit copies of your modified procedures.

You should take prompt action to correct these and any other manufacturing or quality systems deviations identified by your internal audits. Failure to promptly correct these deviations may be identified in a follow-up inspection, and may result in the detention of your device(s) without physical examination upon entry into the United States.

Please notify this office, in writing, within 15 working days of receipt of this letter of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. Please include any and all documentation to show that adequate correction has been achieved. In the case of future corrections, an estimated date of completion, and documentation

showing plans for correction, should be included with your response to this letter. If the documentation is not in English, please provide a translation to facilitate our review. Please address your response and any questions to Timothy R. Wells, Chief, OB/GYN, Gastroenterology and Urology Branch, at the letterhead address.

Should you require any assistance in understanding the contents of this letter, do not hesitate to contact Ms. Sharon Murrain-Ellerbe at the letterhead address or at (301) 594-4616 or FAX (301)594-4638.

Sincerely yours,

Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health